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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,063	02/27/2004	Robert W. Marquis JR.	P50523-C3	7357

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EXAMINER	
TRUONG, TAMTHOM NGO	
ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
07/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,063	MARQUIS ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 15-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,15 and 18* is/are rejected.

7)☒ Claim(s) *16 and 17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4-11-07 has been entered.

Applicant's amendment has overcome the previous rejection of 112/2nd paragraph. Upon review of the amended claims, the following rejections are found necessary.

Claims 12, 14, and 26-33 are cancelled.

Claims 7-11, 13, 19-25 and 34 are withdrawn.

Claims 1-6 and 15-18 are pending.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. **Scope of Enablement:** Claims 1-6, 15 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using compounds of formula I wherein R^4 is mostly $R^5OC(O)$-, does not reasonably provide enablement for making

and using compounds of formula I wherein R^4 is another group . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The breadth of the claims: Claim 1 recites formula I wherein R^1 represents the elected group of R^4-NR'-CHR^3-Z-. Variable R^4 represents several moieties having R^5 which in turn represents an extensive list of moieties and rings or ring systems. With the combination of R^1-R^4 and all possible substituents thereon, formula I encompasses a large number of compounds.

The guidance provided: The specification provides several species of the elected group of formula I in which variable R^4 is mainly $R^5OC(O)$-. Starting materials for adding the side chain (i.e., R^1) are consistent with the group of R^4-NR'-CHR^3-Z- wherein R^4 is $R^5OC(O)$-.

The specification is silent as to the availability of necessary reactants needed to prepare a compound of formula I with a side chain having R^4 as another moiety or a substituent outside of working examples. Note, **In re Howarth** 210 USPQ 689; **Ex parte Moersch** 104 USPQ 122, for the need to show starting material sources commensurate with the claims' scope.

Regarding the biological activity, the specification only details various bioassay methods without specifically indicating which compounds have been tested. Assuming all compounds in the working examples have been tested, their activity cannot be extrapolated to other compounds of formula I wherein the side chain has R^4 as a moiety other than $R^5OC(O)$- as there is no evidence of recognized biological equivalency for such diverse groups.

Thus, the specification does not provide sufficient enablement commensurate with the broad Markush group of formula I.

The state of the prior art: As evident by **Marquis et. al.**, only pyrrolidinone compounds having a side chain corresponding to the elected R^1 in which R^4 is R^5-OC(O)- can inhibit ketone of the cysteine protease cathepsin K.

The relative skill of those in the art: Even with the advanced training, the skilled medicinal chemist and/or clinician would have to carry out extensive research to make an array of compounds of formula I, and select an effective compound from such a large Markush group for inhibiting cysteine protease. Not only one has to determine the inhibitory activity on cysteine protease, but also *in-vivo* activity to establish an LD_{50}, therapeutic index and pharmacokinetic profile for each compound. Given a large Markush group of the claimed formula I, such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The pharmaceutical art has been known for its unpredictability due to various conflicting pathways, or biological factors that are sometimes genetically unique to individuals. In the instant case, the specification does not provide starting materials for making compounds of formula I with various groups represented by R^4 and substituents thereon. It also fails to provide biological data for using all compounds of formula I for inhibiting cysteine protease. The fact that screening for cysteine protease inhibition may be routine does not preclude a finding of nonenablement given the lack of test data and the scope of claims as previously discussed. Note that in **University of Rochester v. G.D. Searle & Co.**, 68 USPQ 2d. 1424 at 1438, the screening for over 600 compounds was deemed to be undue. Applicant's scope far exceeds this number.

Thus, with the large Markush group of formula I, without the guidance for starting material sources of various R^4 groups, undue experimentation is necessary for making such an array of compounds as well as establishing biological activity for said compounds to be cysteine protease inhibitors.

Claim Objections

2. Claims 16 and 17 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Said claims are drawn to species which are not taught or fairly suggested by the prior art of record.

3. **Non-elected Subject Matter:** This application contains claims 1-6 and 15-18 are still drawn to an invention nonelected with traverse in the reply filed on 10-3-05. A complete reply to the rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

References cited on PTO-892

4. The cited US patents (US 6,232,342 and US 5,998,470) show the state of the prior art. While they teach a side chain corresponding to the instant R^1, they fail to teach or fairly suggest the *pyrrolidinyl* or *pyrrolidinone* core.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M, T and Th (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tamthom N. Truong
Examiner
Art Unit 1624

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

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7-19-07